REMARKS

Status of the Claims

Claims 2, 4-10, 24-43, 49-60, 63-66, 68-75 are pending. Claims 69, 71 and 73 are indicated as allowed and Claims 6 and 75 are indicated to be allowable.

Priority

Applicants note that the Office has acknowledged that they are entitled to the benefit of the September 1, 1999 filing date of the '195 provisional application. (Final Office Action, page 2).

Rejections Withdrawn

Applicants note that the Office has withdrawn the previous rejection under 35 U.S.C. § 102(f). (Final Office Action, page 21). The obviousness-type double patenting rejections over 2003/0138453 have also been withdrawn as duplicative of the same rejections over U.S. Application No. 09/967,464. *Id.*

35 U.S.C. § 112, 1st paragraph, Written Description

1. The rejection

Claims 2, 4, 7-10, 24-43, 49-60 and 63-66 were rejected as allegedly not described by the specification as filed. (Final Office Action, pages 2-15). In particular, it was alleged that the written description requirement has not been met because

(a) the genus of polynucleotides is no claimed in a "specific biochemical or molecular structure that could be envisioned by one of skill in the art";

(b) the term "an immunogenic HIV Gag polypeptide" is allegedly not defined and that the polypeptide encoded by the claimed polynucleotides must exhibit all the "numerous and complex" Gag functions;

(c) a "core structure" is not allegedly described;

(d) possession has not been shown because testing for at least "1.1×10^{323}" variants is required; and

(e) possession of the genus has not been shown because the application contains only a "constructive reduction to practice" for some variants.

(a) The Rejection is Premised on Improper Claim Construction

In response to Applicants' amendments to indicate that the claimed sequences encode an "immunogenic HIV Gag polypeptide," the Examiner stated that this term is not defined and that an immunogenic HIV Gag polypeptide is one that must have all the "numerous and complex" roles of an HIV Gag protein. *Id.*

However, the instant claims are not directed to any generically immunogenic polypeptide. Rather, the claimed sequences must encode an immunogenic HIV Gag polypeptide. In other words, the immunogenic response elicited by the encoded polypeptide is a response specific for HIV Gag. The polypeptide is not required to have any other Gag activities – eliciting a Gag specific immune response is sufficient.

As clearly used throughout the specification, the term "immunogenic HIV polypeptide" refers only to HIV Gag polypeptides elicit an immune response. *See, e.g.,* page 14, lines 14-16, where it is clearly noted that an immunogenic polypeptide is one which elicits a humoral and/or cellular immune response "to the antigenic molecule of interest," in this case a immune response to HIV Gag (emphasis added):

> An "immunogenic composition" is a composition that comprises an antigenic molecule where administration of the composition to a subject results in the development in the subject of a humoral and/or cellular immune response to the antigenic molecule of interest.

See, also, page 52, lines 11-22 of the as-filed specification, which clearly indicates that HIV Gag polypeptides encoded by the claimed sequences are immunogenic and that the immunogenicity of the polypeptide can be increased, for example by deleting various regions.

In addition to the fact that the specification clearly teaches that the polypeptide encoded by the claimed sequences is an immunogenic HIV Gag polypeptide, Applicants believe that the Examiner's reading of "immunogenic" out of the context with "HIV Gag polypeptide" renders the claim meaningless and fails to comport with the knowledge of one of skill in the art in the field of HIV and molecular biology.

It was well known at the time of filing that an HIV Gag polypeptide would elicit an immune response specific for HIV Gag, even when the Gag polypeptide did not exhibit "other" Gag functions. *See, e.g.,* WO 00/39302 (Ref FX-1 of IDS filed December 18, 2002 and considered February 13, 2003). To assert that the term "immunogenic HIV Gag polypeptide" is not defined and/or does not limit the scope of the claims on the grounds that all Gag activities must be exhibited stretches the meaning of the claims beyond credulity. The skilled artisan would clearly recognize that an "immunogenic HIV Gag polypeptide" is one that elicits a Gag-specific immune response.

In light of the art, as exemplified by the references discussed above, the term "immunogenic HIV Gag polypeptide" cannot be construed to encompass polypeptides that induce general, non-Gag-specific immune responses.

Indeed, the importance of construing claim language in light of the art was recently reaffirmed by the Federal Circuit, *en banc*, in *Phillips v. AWH*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005). Therein, the court, citing a number of previous decisions,[1] confirmed its precedent that claim terms are given their ordinary and customary meaning to a person of ordinary skill in the art at the effective filing date of the patent application (*Phillips v. AWH Corp.*, 75 USPQ2d 1321, 1326 (Fed. Cir. 2005)):

> We have made clear, moreover, that the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application.

At the time of filing, the skilled artisan was well aware at that date, an "immunogenic HIV Gag polypeptide" would not include polypeptides that did not elicit Gag-specific immune responses.

Thus, the meaning attributed to the term "immunogenic HIV Gag polypeptide" by the Examiner is not the meaning of that term as set forth in the specification or the meaning of the term to one of skill in the relevant art. The claimed sequences encode polypeptides that elicit

[1] See, for example, *Vitronics Corp. v. Conceptronic, Inc.* 90 F.3d 1576, 1582 (Fed. Cir. 1996); *Ferguson Beauregard/Logic Controls v. Mega Sys., LLC*, 350 F.3d 1327, 1338 (Fed. Cir. 2003) and *Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004)

specific (HIV Gag) immune responses and sequences that do not encode polypeptides that produce an HIV Gag-specific immune response are not encompassed by the pending claims. In other words, the genus encompassed by the claims is nowhere near as broad as that painted by the Examiner. When the claims are properly construed, it is plain that they are drawn to a genus of nucleotide sequences encompasses only those nucleotide sequences that encode a polypeptide that elicits a humoral and/or cellular immune response specific for an HIV Gag polypeptide.

(b) A "Core Structure" Does Not Need to be Described

The Examiner has also alleged that adequate written description of a nucleotide sequence requires that the specification describe a "core structure of what is absolutely required for an HIV Gag polypeptide that has 90% sequence identity to the known sequences." (Final Office Action, *e.g.*, page 4).

Applicants submit that the written description rejection cannot be based on an alleged failure to re-describe known molecules, namely immunogenic HIV Gag polypeptides encoded by the claimed polynucleotides.

Indeed, it is axiomatic that a specification need not re-describe known molecules in order to satisfy the written description requirement. See, *Spectra-Physics, Inc. v. Coherent, Inc.* 3 USPQ2d 1737, 1743 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986). Recently, the Federal Circuit in *Falkner v. Inglis,* 79 USPQ2d 1001 (Fed. Cir. 2006), reiterated that reaffirming that adequate written description does not require re-description of the sequence of known molecules and that literature available at the time of filing must be considered in determining the adequacy of the written description (*Falkner*, page 1007-1008, emphasis added):

> Specifically, we hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and **(3) there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure**.

> Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. As we stated in Capon, "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." Id. at 1358. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (wherein permitted) of such genes and sequences.

In the instant case, Applicants are not required to re-describe the sequences of known immunogenic HIV Gag polypeptides in order to satisfy the written description requirement. The claims are directed to novel polynucleotides that encode immunogenic HIV Gag polypeptides. At the time of filing (and indeed to this day), the structure (primary and secondary) of immunogenic HIV Gag polypeptides was well-known to the skilled artisan.

Furthermore, as the written description requirement is highly fact dependent, Applicants reiterate that a "core structure" for immunogenic HIV Gag polypeptides cannot be set forth because the correlation between polypeptide structure (primary sequence or tertiary structure) and specific immunogenic function is not one-to-one. Production of an immune response to an antigen is routinely practiced in the absence of knowledge of a protein's primary or tertiary structure. *See, also,* page 12, lines 3-18 of the as-filed specification regarding epitopes.

See, also, Declaration of Dr. Ulmer, filed January 20, 2004, establishing that it was well-known to the skilled artisan at the time of filing that immunogenicity of HIV Gag polypeptides does not correlate with a core structure (Ulmer Declaration, ¶18, emphasis added):

> 18. Third, the specification unambiguously and clearly describes at the time of filing, the correlation between structure of the claimed biomolecules and their immunogenic function. ... Furthermore, those of us working in this field knew, at the time of filing, that **any given antigen can tolerate a number of amino acid substitutions while still retaining its immunogenic function. In**

> **other words, a particular amino acid sequence is not required in order to elicit a *Gag*-specific immune response. Rather, one would expect that a multitude of *Gag* polypeptides, having different amino acid sequences, would function to generate specific an immune response in a subject.** Thus, it would have been clear to the skilled worker that the specification describes the correlation between the structure and function set forth in the claims.

One of skill in the art can routinely produce antibodies that specifically bind to a protein by immunizing an appropriate host with oligopeptide fragments of that protein. It is well known in the art that it is possible to produce antibodies to almost any part of an antigen, and is not especially difficult to obtain antibodies with specificity for a particular protein, as set forth in the claims. Moreover, a specific cellular immune response is also routinely produced by immunization with antigen. The specification provides amply guidance for one of skill in the art to elicit an immune response (*i.e.*, humoral and/or cellular) with the recited polynucleotides encoding HIV Gag polypeptides that elicit a Gag-specific immune response. *See*, specification, *e.g.*, at Examples 4, 5 and 7.

Simply put, not only is a core structure not describable for immunogenic HIV Gag polypeptides, the written description requirement does not necessitate that Applicants re-describe known immunogenic HIV Gag polypeptides that are encoded by their novel polynucleotides.

(c) Possession of the Genus is not Determined by the Amount of Testing Required

The Examiner also alleges that the skilled artisan would not know how to determine sequences that encode an HIV Gag polypeptide on the grounds that over 1.1×10^{323} variants would have to be tested and that the possibility of such testing does not evince possession. (Final Office Action, pages 4 and 13).

The Examiner's assertion that testing establishes that the specification lacks an adequate written description is legally and factually erroneous.

Legally, the amount or nature of any "testing" is not a factor considered in assessing the adequacy of description. *See, e.g., Capon v. Eshhar,* 76 USPQ2d 1078, 1085-1086 (Fed. Cir. 2005):

> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. ...
>
> Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. [citations omitted].
>
> It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. See In re Angstadt, 537 F.2d 498, 504 [190 USPQ 214] (CCPA 1976) ("The examples, both operative and inoperative, are the best guidance this art permits, as far as we can conclude from the record"). While the Board is correct that a generic invention requires adequate support, the sufficiency of the support must be determined in the particular case. Both Eshhar and Capon present not only general teachings of how to select and recombine the DNA, but also specific examples of the production of specified chimeric genes.
>
> The PTO points out that for biochemical processes relating to gene modification, protein expression, and immune response, success is not assured. However, generic inventions are not thereby invalid.

As repeatedly noted, and admitted by the Examiner in dismissing the relevance of *Capon,* a written description inquiry is highly fact-dependent. The facts in this case establish Applicants have provided more than adequate guidance for obtaining the claimed polynucleotides, including "testing" of any number of different sequences. With respect to the alleged large number of variants that must be tested, Applicants note that the skilled artisan would know, well prior to testing, that many of these sequences would not encode polypeptides (*e.g.,* if they contain a stop codon near the start site).

Regardless of the number of variants, Applicants reiterate that the as-filed specification teaches, in detail and with working examples, how to obtain the claimed polynucleotides. Each and every member of the claimed genus – be it 2 or 2 billion members in size – is **literally** described in the as-filed specification. Satisfaction of the written description requirement does not necessitate that each and every member of the claimed genus be set forth, let alone "tested" in order to show possession. Nor does the written description requirement necessitate a showing that the skilled artisan can predict *a priori* each and every nucleotide sequence falling within the

scope of the claims. Even if it did, Applicants have met this inasmuch as the as-filed specification contains unambiguous **literal** description of the structure of any member of the claimed genus by reference to its sequence similarity to a reference sequence.

Thus, the process for "testing" the polypeptides encoded by the claimed sequences is much more than possible, it is amply described in sufficient detail to demonstrate that Applicants were in possession, at time of filing, of any nucleotide sequence that exhibits 90% identity to SEQ ID NOs:3 or 4 and which encodes an HIV Gag polypeptide that elicits an Gag-specific immune response in a subject.

(d) Reduction to Practice is Not Required to Satisfy the Written Description Requirement

The Examiner also alleges that actual reduction to practice of a single (or few) species is not sufficient in the present case to establish possession because of the alleged "lack of information regarding numerous possible variants of known sequences." (Final Office Action, pages 4-6).

For the reasons of record and reiterated herein, the Examiner also errs in asserting that insufficient representative species are actually reduced to practice. It is well settled that description of a single species can provide an adequate description, even for a broad genus. Description does not require exemplification. *See, Capon v. Eshhar* 76 USPQ2d 1078 (CA FC 2005):

> It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. *See In re Angstadt*, 537 F.2d 498, 504 [190 USPQ 214] (CCPA 1976) ("The examples, both operative and inoperative, are the best guidance this art permits, as far as we can conclude from the record"). While the Board is correct that a generic invention requires adequate support, the sufficiency of the support must be determined in the particular case. ...

See, also, Falkner v. Inglis, in which the Federal Circuit cited *Capon* in reiterating that actual reduction to practice is not required (*Falkner,* at 1007-1008):

> Specifically, we hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description **(2) the written description standard may be met (as it is here) even where actual reduction**

> **to practice of an invention is absent**; and (3) there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure. ...
>
> As we explained in *Capon v. Eshhar*, "[t]he 'written description' requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed." 418 F.3d 1349, 1357 [76 USPQ2d 1078] (Fed. Cir. 2005). ....
>
> Thus, to the extent that written description requires a showing of "possession of the invention," *Capon*, 418 F.3d at 1357 (emphasis added), [it is] clear that **an invention can be "complete" even where an actual reduction to practice is absent**.

These are clear, fact-independent holdings of the Federal Circuit. Thus, a specification need not describe every polynucleotide permutation in order for an inventor to obtain a generic claim and actual reduction to practice of polynucleotides falling within the scope of the claims is never necessary for compliance with the written description requirement.[2]

In any event, the as-filed specification has in fact exemplified that sequences comprising the claimed reference sequence that encode immunogenic HIV Gag polypeptides. In fact, the exact sequence of reference sequences SEQ ID NOs:3 and 4 are literally described in the as-filed specification, it is clear that Applicants were in possession of not only these molecules but, in addition, nucleotides exhibiting 90% identity to these molecules.

The as-filed specification establishes skilled artisan can envision the detailed structure of every single member of the claimed genus (a polynucleotide exhibiting 90% identity to the recited reference sequence). The specification describes, in detail, how HIV Gag polypeptides are identified, for example by Western blotting, ELISA or the like and how to determine immunogenicity. (See, *e.g.*, Examples).

Further, contrary to the Examiner's assertion (*e.g.*, page 5 of the Final Office Action), the sequences (including "critical" epitopes) of various HIV Gag-encoding polynucleotides (as well

[2] *See, also,*, the PTO Guidelines, favorably commented on by the Federal Circuit, include various Examples that establish that claims to a genus of sequences are properly described if (1) the DNA sequence is novel, (2) unobvious, and (3) a specific activity is recited. *See,* Examples 9 and 14 of the PTO Guidelines on Written Description, reproduced in the Response filed September 26, 2005.

as Gag polypeptides themselves) were known at the time of filing and are described, for example, in the Background section and references cited therein.

The test for determining satisfaction of the requirement of Section 112, 1st paragraph is not what sequences are actually reduced to practice in the as-filed specification, but, rather, what the disclosure as a whole and available knowledge to determine whether the specification as-filed evinces possession of the claimed subject matter to the skilled artisan. The skilled artisan, having followed the teaching of the specification, would have no doubts that Applicants were in possession of the claimed subject matter (and that the as-filed specification teaches how to make and use the claimed sequences).

Therefore, for the reasons of record and those set forth herein, the as-filed specification more than satisfies the written description requirement of 35 U.S.C. § 112, 1st paragraph.

(e) Eli Lilly

The Examiner also again asserted that the arguments regarding cited case law were not found persuasive (Final Office Action, page 5).

However, the underlying fact-pattern (*e.g.,* disclosure) is what matters in determining written description and the claims and disclosure of the pending case are completely different than the claims and disclosure at issue in *Regents of the Univ. Calif. v. Eli Lilly.*

The pending claims are drawn to sequences having 90% identity to a particular **reference** sequence. The claims in *Eli Lilly* did not recite a reference sequence for the simple reason that **no** reference sequences were disclosed. Instead, the claims in *Lilly* were directed to any sequence encoding human insulin. In addition, there was no disclosure in *Lilly* of any cDNA sequences encoding human insulin.

In fact, unlike *Lilly,* the subject matter claimed in the present application is not a single sequence encoding a known protein. Rather, the pending claims, by their very nature, encompass a variety of sequences having the recited structure and function. Unlike *Lilly*, Applicants' specification includes examples of sequences and these examples have the requisite degree of specificity (setting forth particular nucleotides). Accordingly, the skilled artisan is able to predict *a priori* the nucleotide sequence of each and every species encompassed by the claims

and, in addition, would be aware Applicants were in possession of methods for making such sequences.

Thus, whereas Applicants' as-filed specification discloses at least six representative examples and the claims recite a reference sequences, *Lilly* fails to disclose any representative species and, accordingly, could not recite a reference sequence in the claims. The holding in *Lilly* is not that claims encompassing a genus of sequences can never be described but, rather, that the disclosure in *Lilly* fails to adequately describe the particular claims at issue. When properly evaluated, it is clear that Applicants' as-filed disclosure fully describes the claimed sequences.

35 U.S.C. § 112, 1st Paragraph, Enablement

As set forth in the seminal case of *In re Marzocchi,* 439 F.2d, 220, 223, 169 USPQ 367, 369 (CCPA 1971), a patent application is presumptively enabled when filed:

> [a]s a matter of Patent Office practice ... a specification .. must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Moreover,

> it is incumbent upon the Patent Office, whenever a rejection on [grounds of enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

439 F.2d at 224, 169 USPQ at 369-370. Indeed, as pointed in the Patent Office's own Training Manual on Enablement (1993, citing *In re Wright,* 999 F.2d 1557, 1561-1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993), "the case law makes clear that properly reasoned and supported statements explaining any failure to comply with section 112 are a requirement to support a rejection."

In the pending case, the Examiner has supported the enablement rejection by citing Freed, Baker, Attwood, Gerhold, Russel, Wells and Ngo, which were alleged to demonstrate the

unpredictability of polynucleotides encoding polypeptides exhibiting "the biological function of a wild-type Gag polypeptide." (Final Office Action, page 5 and 11). However, these references do not provide a properly reasoned and supported basis for finding non-enablement.

Freed, which allegedly demonstrates that a Gag protein has "numerous" and "complex" roles, is not germane to the claims as pending. The polynucleotides of the claims are not required to have all Gag activities. Rather, all that is required is that the polynucleotides exhibit the requisite identity to the references sequences and encode a polypeptide that elicits a Gag-specific immune response. As noted above and throughout prosecution, the specification at issue provides ample guidance in this regard, for example, on page 14 and references cited therein. Accordingly, Freed is not relevant to the pending claims.

Baker, Attwood, Russell and Ngo are cited for allegedly showing unpredictability of the relationship of primary, secondary and tertiary structure of a polypeptide. However, as noted above, a Gag-specific immune response can be generated by short epitopes and, accordingly, there is no need to predict, a priori, the "structure" or "folding" of a polypeptide encoded by the claimed molecules.

Likewise, Gerhold and Wells relate to methods of determining gene function based on EST sequence. This is not relevant to the pending claims, in which the only function required by the polypeptide is that elicits a Gag-specific immune response and which required function does not necessitate the entire coding sequence or core structures.

The relevant question regarding enablement remains what the specification and state of the art at the time of filing teaches one of skill in the art in regard to eliciting Gag-specific immune responses. The disclosures of Freed, Baker, Attwood, Gerhold, Russel, Wells and Ngo do not change the fact that any experimentation needed to polynucleotides exhibiting 90% sequence identity to SEQ ID NOs:3 and 4 and which encode an immunogenic Gag polypeptide is utterly routine in view of the teachings of the specification and the state of the art. The Office has not provided sufficient evidence supporting non-enablement and, in the absence of necessary relevant evidence contradicting the teachings of the specification and state of the art, the rejection cannot be maintained.

(a) Undue Experimentation is Not Required to Make and Use the Claimed Polynucleotides

Applicants remind the Office that it is well settled that even time-consuming or expensive experimentation is **not** undue if it is routine. (See, *e.g.,* PTO Training Manual on Enablement, pages 30-31, citing *United States v. Telectonics Inc.,* USPQ2d 1217, 1223 (Fed. Cir. 1988), *cert. denied* 490 U.S. 1046 (1989) holding the disclosure of a single exemplified embodiment and a method to determine other embodiments was enabling, even in the face of evidence that determining additional embodiments might require 6-12 months of effort and cost over $50,000). Furthermore, the notion that one of ordinary skill in the art must have reasonable assurance of obtaining an active claimed product has been emphatically rejected by the courts. *See, Angstadt* at 219. So long as it is clear that some species render a composition operative, the inclusion of some possible inoperative species does not invalidate the claim under paragraph 1, of 35 U.S.C. §112. *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, CCPA 1971; *Horton v. Stevens*, 7 USPQ2d 1245, 1247, Fed. Cir. 1988.

In the instant case, the specification discloses the precise sequence of the reference sequences, how to determine sequences having 90% identity to these reference sequences, how to express a polypeptide from the polynucleotides having the requisite sequence homology, and The actual scope of the claims, and the nature of the guidance provided in the specification (*e.g.*, at Examples 2-7 and Sections 2.1.3 and 2.3), along with the conventional nature of methods of modifying sequences and determining their function, all establish that the specification as filed fully enables the claims.

Moreover, the clear teachings of the specification are supplemented by further evidence of the routine nature of making and using the claimed polynucleotides. In particular, as noted above, WO 00/39302 (Ref FX-1 of IDS filed December 18, 2002 and considered February 13, 2003, now U.S. Patent No. 6,602,705, which demonstrates that synthetic polynucleotides similar to those claimed (but for Type B HIV) encode immunogenic Gag polypeptides. Applicants are not required to show perfect efficiency or success rates. All that is required is that one of skill in the art could make and use the claimed polynucleotides. The specification and evidence of record plainly demonstrate that this requirement has been met.

In sum, given the clear teachings in the specification and the high level of knowledge at the time of filing, it would not require undue experimentation to make and use polynucleotides as claimed. Furthermore, for the reasons of record and reiterated above, the references cited by the Office do not provide any reasons to doubt that the skilled artisan could make and use the claimed molecules.

Declaratory Evidence Relevant to Both Enablement and Written Description Has Not Been Properly Considered

As noted above and previously, the Declarations of Drs. Donnelly and Ulmer, previously submitted on December 18, 2002 and January 20, 2004 (respectively) have not been adequately considered. In point of fact, these declarations further establish that the sequences having at least 90% identity to SEQ ID NO:3 or SEQ ID NO:4 are both enabled and described by the as-filed specification.

Drs. Donnelly and Ulmer attest to the fact that the specification enables one of one of skill in the art to make and use the claimed subject matter. *See,* Donnelly Declaration, ¶7 and ¶8 and Ulmer Declaration, ¶11 and ¶12).

With regard to written description of "core" or "essential regions", as previously noted and reiterated above, Dr. Ulmer establishes that immunogenicity does is not directly correlated with either primary or tertiary structure

Thus, using specific facts, Drs. Donnelly and Ulmer conclude that the as-filed specification describes and enables the claimed subject matter. This convincing, factual evidence has been improperly dismissed by the Office (*see, e.g., In re Alton,* 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

Thus, for the reasons of record and above, the specification describes and enables the claimed subject matter. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Provisional Rejections Under Nonstatutory-Type Double Patenting

The Office has maintained several provisional rejections under the judicially created doctrine of obviousness-type double patenting. These provisional rejections are as follows:

A) Claims 2, 4, 5, 24, 25, 41-43, 68 and 74 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50 and 72 of copending U.S. Application No. 09/967,464 ('464).

B) Claims 2, 24 and 25 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 26, 28, 31-50 and 72 of the '464 application in view of Tartaglia et al. (U.S. Patent No. 5,990,091) and Corbin et al. (U.S. Patent No. 6,489,542).

C) Claims 2 and 24-26 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 26, 28, 31-50 and 72 of the '464 application in view of Tartaglia et al. (U.S. Patent No. 5,990,091) and Corbin et al. (U.S. Patent No. 6,489,542) and either Sikic et al. (U.S. Patent No. 5,830,697) or Dubensky et al. (U.S. Patent No. 6,391,632).

D) Claims 2 and 27-40 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50 and 72 of the '464 application in view of ATCC catalog of cell lines and hybridomas (7^{th} edition, Maryland, 1992, pages 70, 79, 148, 150, 158, 164, 194, 299, 308 and 456); Helting et al. (U.S. Patent No. 5,470,720); and Adams et al. (IJ-1).

E) Claims 68 and 70 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50 and 72 of the '464 application in view of Rovinski et al. (BS-1).

F) Claims 68 and 72 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50 and 72 of the '464 application in view of Rovinski et al. (BE-1).

The Examiner has acknowledged that the present application is entitled to a priority date of September 1, 1999. The earliest priority date for the '464 application (upon which all the obviousness-type double patenting rejections) is September 28, 2000. Thus, the present

application is the earlier filed application. As set forth in MPEP § 804, a provisional nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of the two pending applications, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer (*See* MPEP § 804(I)(B)(1)).

Furthermore, as each of these rejections are *provisional* rejections, Applicants request that they be held in abeyance until there is an indication of allowable subject matter in either the present application or in the '464 application.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is in condition for allowance. If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

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